

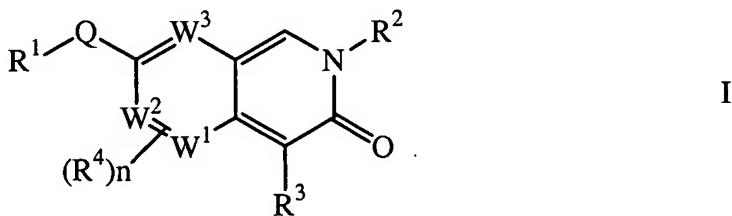
### AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of claims:**

**Claim 1 (currently amended).**

A compound of Formula I



or a pharmaceutically acceptable salt thereof,

wherein:

R<sup>1</sup> is independently selected from:

- C<sub>5</sub> or C<sub>6</sub> cycloalkyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Substituted C<sub>5</sub> or C<sub>6</sub> cycloalkyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- C<sub>8</sub>-C<sub>10</sub> bicycloalkyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Substituted C<sub>8</sub>-C<sub>10</sub> bicycloalkyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- 5- or 6-membered heterocycloalkyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Substituted 5- or 6-membered heterocycloalkyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- 8- to 10-membered heterobicycloalkyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Substituted 8- to 10-membered heterobicycloalkyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Phenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Substituted phenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Naphthyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Substituted naphthyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- 5- or 6-membered heteroaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Substituted 5- or 6-membered heteroaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- 8- to 10-membered heterobiaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl); and
- Substituted 8- to 10-membered heterobiaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);

Phenyl;  
Substituted phenyl;  
Naphthyl;  
Substituted naphthyl;  
5- or 6-membered heteroaryl;  
Substituted 5- or 6-membered heteroaryl;  
8- to 10-membered heterobiaryl;  
Substituted 8- to 10-membered heterobiaryl;

$R^2$  is independently selected from:

H;  
 $C_1\text{-}C_6$  alkyl;  
Phenyl-( $C_1\text{-}C_8$  alkylenyl);  
Substituted phenyl-( $C_1\text{-}C_8$  alkylenyl);  
Naphthyl-( $C_1\text{-}C_8$  alkylenyl);  
Substituted naphthyl-( $C_1\text{-}C_8$  alkylenyl);  
5- or 6-membered heteroaryl-( $C_1\text{-}C_8$  alkylenyl);  
Substituted 5- or 6-membered heteroaryl-( $C_1\text{-}C_8$  alkylenyl);  
8- to 10-membered heterobiaryl-( $C_1\text{-}C_8$  alkylenyl); and  
Substituted 8- to 10-membered heterobiaryl-( $C_1\text{-}C_8$  alkylenyl);  
Phenyl-O-( $C_1\text{-}C_8$  alkylenyl);  
Substituted phenyl-O-( $C_1\text{-}C_8$  alkylenyl);  
Phenyl-S-( $C_1\text{-}C_8$  alkylenyl);  
Substituted phenyl-S-( $C_1\text{-}C_8$  alkylenyl);  
Phenyl-S(O)-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted phenyl-S(O)-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Phenyl-S(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted phenyl-S(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);

Each substituted  $R^1$  and  $R^2$  group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

$C_1\text{-}C_6$  alkyl;  
CN;

CF<sub>3</sub>;

HO;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-O;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-S(O)<sub>2</sub>;

H<sub>2</sub>N;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-N(H);

(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>-N;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)O-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)O-(1- to 8-membered heteroalkylenyl)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)N(H)-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)N(H)-(1- to 8-membered heteroalkylenyl)<sub>m</sub>;

H<sub>2</sub>NS(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);

(C<sub>1</sub>-C<sub>6</sub> alkyl)-N(H)S(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>-NS(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)<sub>m</sub>;

3- to 6-membered heterocycloalkyl-(G)<sub>m</sub>;

Substituted 3- to 6-membered heterocycloalkyl-(G)<sub>m</sub>;

5- or 6-membered heteroaryl-(G)<sub>m</sub>; and

Substituted 5- or 6-membered heteroaryl-(G)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-S(O)<sub>2</sub>-N(H)-C(O)-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)<sub>m</sub>;

(C<sub>1</sub>-C<sub>6</sub> alkyl)-C(O)-N(H)-S(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)<sub>m</sub>;

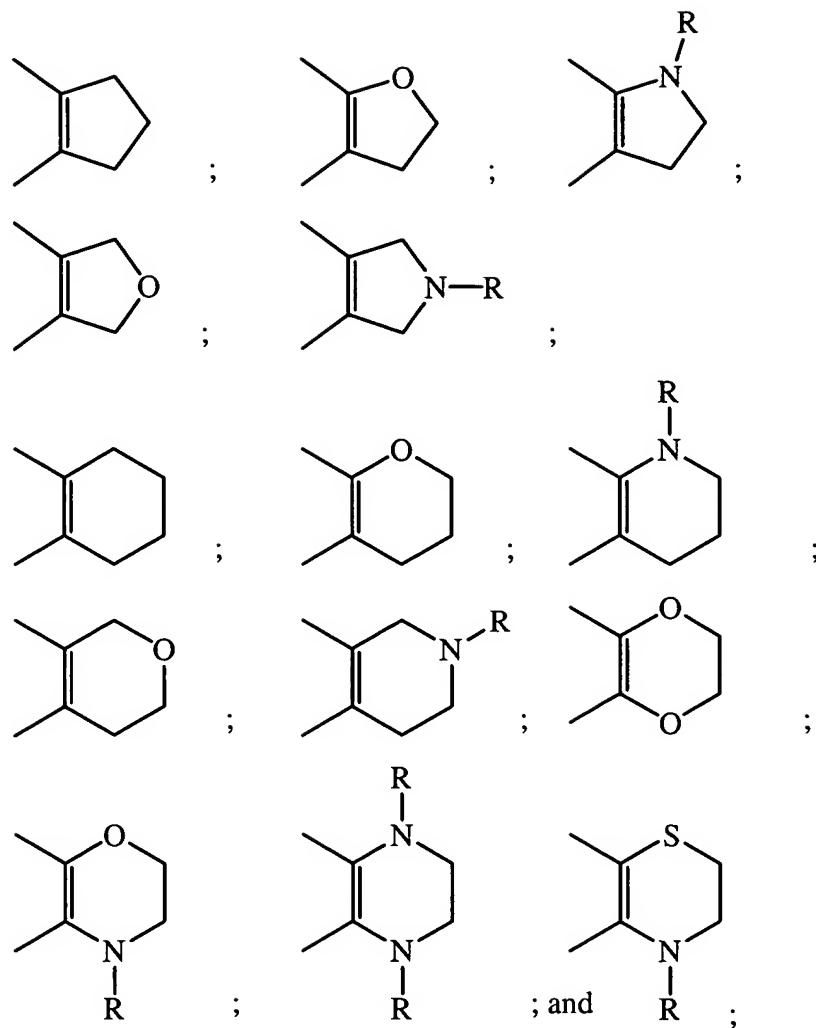
wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

HO<sub>2</sub>C;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially sp<sup>2</sup> carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:



R is H or C<sub>1</sub>-C<sub>6</sub> alkyl;

G is CH<sub>2</sub>; O, S, S(O); or S(O)<sub>2</sub>;

Each m is an integer of 0 or 1;

R<sup>3</sup> is selected from the groups:

H;

C<sub>1</sub>-C<sub>6</sub> alkyl;

Substituted C<sub>1</sub>-C<sub>6</sub> alkyl;

C<sub>2</sub>-C<sub>6</sub> alkenyl;

Substituted C<sub>2</sub>-C<sub>6</sub> alkenyl;

C<sub>2</sub>-C<sub>6</sub> alkynyl;

Substituted C<sub>2</sub>-C<sub>6</sub> alkynyl;

C<sub>3</sub>-C<sub>6</sub> cycloalkyl;

Substituted C<sub>3</sub>-C<sub>6</sub> cycloalkyl;  
C<sub>3</sub>-C<sub>6</sub> cycloalkyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted C<sub>3</sub>-C<sub>6</sub> cycloalkyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Phenyl;  
Substituted phenyl;  
Phenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted phenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Naphthyl;  
Substituted Naphthyl;  
Naphthyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted naphthyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
3- to 6-membered heterocycloalkyl;  
Substituted 3- to 6-membered heterocycloalkyl;  
3- to 6-membered heterocycloalkyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);  
Substituted 3- to 6-membered heterocycloalkyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl)  
HO;  
(C<sub>1</sub>-C<sub>6</sub> alkyl)-O;  
H<sub>2</sub>N;  
(C<sub>1</sub>-C<sub>6</sub> alkyl)-N(H);  
(C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>-N;

Each substituted R<sup>3</sup> group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

H<sub>2</sub>N;  
C<sub>1</sub>-C<sub>6</sub> alkyl;  
CN;  
CF<sub>3</sub>;  
(C<sub>1</sub>-C<sub>6</sub> alkyl)-OC(O);  
HO;  
(C<sub>1</sub>-C<sub>6</sub> alkyl)-O;  
HS; and  
(C<sub>1</sub>-C<sub>6</sub> alkyl)-S;

wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

$\text{HO}_2\text{C}$ ;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group  $\text{C}=\text{O}$ ;

$\text{R}^4$  is H,  $\text{C}_1\text{-}\text{C}_6$  alkyl,  $\text{H}_2\text{N}$ , HO, or halo;

n is an integer of from 0 to 3;

Q is selected from:

$\text{OC(O)}$ ;

$\text{CH(R}^5\text{)C(O)}$ ;

$\text{OC(NR}^5\text{)}$ ;

$\text{CH(R}^5\text{)C(NR}^5\text{)}$ ;

$\text{N(R}^5\text{)C(O)}$ ;

$\text{N(R}^5\text{)C(S)}$ ;

$\text{N(R}^5\text{)C(NR}^5\text{)}$ ;

$\text{N(R}^5\text{)CH}_2$ ;

$\text{SC(O)}$ ;

$\text{CH(R}^5\text{)C(S)}$ ;

$\text{SC(NR}^5\text{)}$ ;

trans-(H) $\text{C}=\text{C(H)}$ ;

cis-(H) $\text{C}=\text{C(H)}$ ;

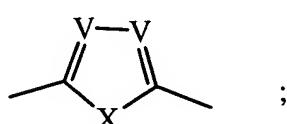
$\text{C}\equiv\text{C}$ ;

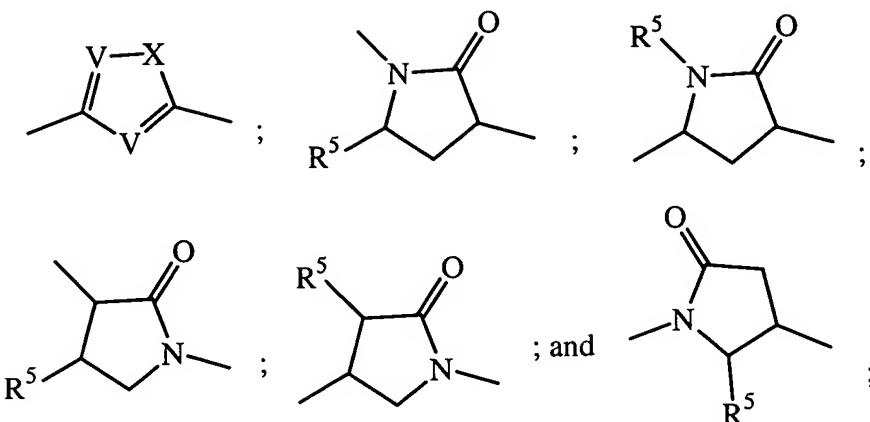
$\text{CH}_2\text{C}\equiv\text{C}$ ;

$\text{C}\equiv\text{CCH}_2$ ;

$\text{CF}_2\text{C}\equiv\text{C}$ ; and

$\text{C}\equiv\text{CCF}_2$ ;





$R^5$  is H, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl; 3- to 6-membered heterocycloalkyl; phenyl;

benzyl; or 5- or 6-membered heteroaryl;

X is O, S, N(H), or N(C<sub>1</sub>-C<sub>6</sub> alkyl);

Each V is independently C(H) or N;

Each W<sup>1</sup>, W<sup>2</sup>, and W<sup>3</sup> is independently N or C R<sup>4</sup>, wherein R<sup>4</sup> is as defined above;

One of W<sup>1</sup>, W<sup>2</sup>, and W<sup>3</sup> is N and the other two of W<sup>1</sup>, W<sup>2</sup>, and W<sup>3</sup> are each C-R<sup>4</sup>,  
wherein R<sup>4</sup> is as defined above;

wherein each C<sub>8</sub>-C<sub>10</sub> bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)<sub>2</sub>, 1 N, 4 N(H), and 4 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)<sub>2</sub>, 1 N, 4 N(H), and 4 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded

to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;  
wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;  
wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C<sub>1</sub>-C<sub>6</sub> alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;  
wherein with any (C<sub>1</sub>-C<sub>6</sub> alkyl)<sub>2</sub>-N group, the C<sub>1</sub>-C<sub>6</sub> alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and  
wherein each group and each substituent recited above is independently selected.

**Claims 2 and 3 (cancelled).**

**Claim 4 (original).** The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is N(R<sup>5</sup>)C(O) or C≡C.

**Claim 5 (original).** The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is C≡C.

**Claim 6 (original).** The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein n is 0.

**Claim 7 (original).** The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein n is 1.

**Claim 8 (currently amended).** The compound according to any one of ~~Claims 1 to 7~~ Claims 1 or 4 to 7 inclusive, or a pharmaceutically acceptable salt thereof, wherein R<sup>1</sup> is independently selected from:

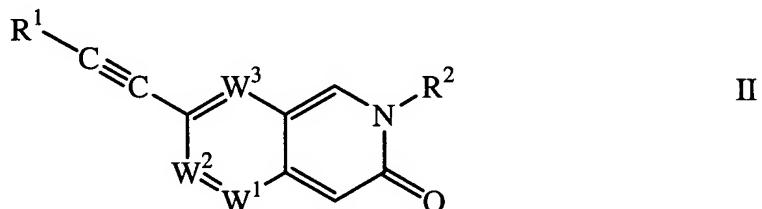
- 5- or 6-membered heteroaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Substituted 5- or 6-membered heteroaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- 8- to 10-membered heterobiaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Substituted 8- to 10-membered heterobiaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Phenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl); and
- Substituted phenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl); and

R<sup>2</sup> is independently selected from:

- 5- or 6-membered heteroaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Substituted 5- or 6-membered heteroaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- 8- to 10-membered heterobiaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Substituted 8- to 10-membered heterobiaryl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);
- Phenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl); and
- Substituted phenyl-(C<sub>1</sub>-C<sub>8</sub> alkylenyl);

wherein each group and each substituent is independently selected.

**Claim 9 (original).** The compound of Claim 1 of Formula II



or a pharmaceutically acceptable salt thereof.

**Claim 10 (cancelled).**

**Claim 11 (original).** A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

**Claim 12 (cancelled).**

**Claim 13 (original).** A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

**Claim 14 (cancelled).**

**Claim 15 (new).** The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein W<sup>2</sup> is N and W<sup>1</sup> and W<sup>3</sup> are each C-R<sup>4</sup>, wherein R<sup>4</sup> is as defined above.